OTS: 60-41,359

JPRS: 5547

19 September 1960

AMINORASTIN -- A NEW SOLUTION FOR PARENTERAL PROTEIN FEEDING

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- USSR -

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Price: ~~$0.50~~

U. S. JOINT PUBLICATIONS RESEARCH SERVICE
205 EAST 42nd STREET, SUITE 300
NEW YORK 17, N. Y.

JPRS: 5547

CSO: 4570-N

AMINORASTIN -- A NEW SOLUTION FOR PARENTERAL PROTEIN FEEDING

/Following is the translation of an article by Senior Scientific Coworker M. Ye. Depp and Candidate of Biological Sciences T. V. Znamenskaya entitled "Aminorastin -- Novyy Rastvor Dlya Parenteral'nogo Belkvogo Pitaniya" (English version above) in Vestnik khirurgii imeni I. I. Grekova (Herald of Surgery imeni I. I. Grekova), Vol. LXXXV, No. 5, 1960, pages 64-67./

From the Blood Substitutes Laboratory (Head -- Professor L. G. Bogomolova) and the Surgical Clinic (Scientific Director -- Professor A. N. Filatov) of Leningrad Order of Labor Red Banner Institute of Blood Transfusion.

At the present time hydrolyzates of various proteins are being used widely in surgical practice for parenteral protein feeding. The method of hydrolysis permits solutions to be obtained from heterogeneous proteins which do not possess antigenic and toxic properties and which are excellently assimilated when introduced into the organism.

In 1955 in the Laboratory of Blood Substitutes of Leningrad Institute of Blood Transfusion, a method of preparing a hydrolyzate from protein of plant origin was worked out (T. V. Znamenskaya). Proteins of plants are full-value proteins, i. e., contain in their composition all the essential amino acids. Aminorastin solution, containing amino acids, peptides, glucose, and salts, was obtained from plant protein via acidic hydrolysis. The total nitrogen content in the solution amounts to 0.6-0.8%; the amino nitrogen content -- to 0.3-0.4%.

In its chemical composition aminorastin is identical with the solution previously proposed by Leningrad Blood Transfusion Institute -- hydrolyzin (I. R. Petrov, L. G. Bogomolova, Z. A. Chaplygina) and aminokrovin (Z. A. Chaplygina). The study of the amino acid composition of aminorastin by the method of distribution chromatography on paper has shown that this solution contains those same amino acids which were found in hydrolyzates of proteins of animal origin

-- the hydrolyzin and aminokrovin solutions (Z. A. Chaplygina, T. V. Znamenskaya).

The experimental testing of the biological properties of aminorastin has shown that the solution does not give rise to toxic and antigenic reactions. Our investigations have also shown that when aminorastin was administered for a long time to rabbits in a quantity of 10 ml per kg of body weight, no toxic or cumulative phenomena were detected in them. No deviations from normal were found in the histological investigation of the organs of these rabbits (liver, kidney, spleen, and heart). The assimilability of aminorastin was studied in experiments on dogs which were on a protein-free diet. The administration of the solution intravenously or subcutaneously created a positive nitrogen balance in the organism.

The infusion of aminorastin was performed in the surgical clinic of the Institute; 145 infusions to 53 patients were performed under our observation, a total quantity of 80 liters. At the present time 250 liters of aminorastin have been prepared in the blood substitutes laboratory of the Institute, which material is being studied in various clinics of the Soviet Union.

The clinical observations had the object of elucidating whether the solution possesses toxic and antigenic properties, whether the nitrogen products of the cleaved plant protein which are being administered are assimilated and whether the administration of aminorastin with the object of parenteral protein feeding is possible. Our first observations have already shown that aminorastin is well endured by patients and does not induce complications either in the presence of intravenous, or in the presence of subcutaneous administration. The solution was administered in a quantity of from 200 to 900 ml and greater, most frequently the doses being administered amounted to 500-700 ml (Table 1).

Table 1

Quantities of aminorastin used in the clinic

Quantity of the solution which was administered (in ml)	200-290	300-490	500-690	700-900	1,000 and greater
Number of infusions	37	20	47	35	6

Table 2

Number of repeated infusions of aminorastin

Number of infusions	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Number of patients	26	2	5	13	5	—	—	—	1	—	—	—	—	1	53

The repeated administration of the solution (Table 2), performed with intervals from two to 10 days, did not induce any side reactions. This confirms the conclusion previously drawn to the effect that the solution does not possess any toxic or antigenic properties.

It should be noted, however, that the administration of aminorastin should be performed in drops at a rate of around 40 drops per minute, i. e., somewhat more slowly, than the administration of the other hydrolyzates. An increase in the rate of administration of the solution can be accompanied by nausea, flushing of the face, pain along the course of the vein, etc. These phenomena disappear when the rate of administration of the solution is diminished. The optimal rate of administration of the solution amounts to 30-60 drops per minute, depending on the individual peculiarities of the organism. The content of the quantity of nitrogen in the preparation also has significance. Those series of solution in which the total nitrogen content was 0.5-0.6%, induced no reactions when the rate of administration was 80 drops per minute.

To elucidate the influence of aminorastin on the blood coagulating system, Z. D. Fedorova and M. A. Kotovshchikova conducted a study of certain indexes of the blood coagulation when the solution was administered. In an investigation of the blood coagulation time, the prothrombin time of the plasma and of the serum, the retraction of the clot in castor oil, and the content of fibrinogen at various periods (24 and 42 hours) after the intravenous administration of aminorastin, no devia-

tions from normal were successfully detected.

To study the assimilability of aminorastin in patients subjected to operative intervention, the nitrogen balance, the amino nitrogen balance, the content of urea in the urine and of protein in the blood serum were studied in the postoperative period. Twenty-three of these patients had received an infusion of aminorastin in a quantity of 250-1,500 ml in the preoperative period as preparation for the operation. After the operation, aminorastin was administered to 25 patients for three days with the object of parenteral feeding. No food was received by the patients in this time. The quantity of solution administered daily amounted to 500-900 ml, which corresponded to 20-30 g of protein. In addition, the patients received vitamins, a solution of glucose and physiological solution to a total volume of the administered liquid of 2.5-3.0 liters. Aminorastin can be administered in combination with various salt solutions, with preserved blood and serum.

According to the data obtained (Table 3), in all patients after operative intervention and the administration of aminorastin, a negative balance of the total nitrogen and a positive balance of the amino nitrogen were observed. The quantity of nitrogen being introduced with the solution was always less than the quantity of nitrogen being excreted with the urine. The magnitude of the negative balance of the total nitrogen fluctuated within limits of -0.5 -- -14.0 g per day, on the average -- 8.6 g. The amino nitrogen balance amounted to from + 3.2 to + 1.0 g per day.

We have compared these data with the data obtained in a control group -- in six individuals who after analogous operative interventions had received only salt solutions and a solution of glucose. The magnitude of the negative balance of total nitrogen in the patients of the control group was somewhat higher -- from -7.0 to +18.5 g of nitrogen per day (on the average - 12.1 g). The amino nitrogen balance in all patients of the control group, in contrast to the patients who had received aminorastin, was negative (from -1.0 to -2.0 g of amino nitrogen per day).

Thus, the administration of aminorastin to patients in the postoperative period lowers the excretion of total nitrogen and creates a positive balance of amino nitrogen in the organism, which is evidence, apparently, of assimilation of the nitrogenous substances being administered.

It should be noted that in all the patients examined by us, nonidentical magnitudes of the negative nitrogen balance were observed. In analyzing the data obtained we have established that this was not associated with the age of the patients and did not depend on the quantity of solution administer-

Table 3

Nitrogen balance of the patients in the presence of the administration of aminorastin

Surname of the patient	Age in Years	Average amount of nitrogen excreted per day (in g)	Average amount of nitrogen administered per day (in g)	Average daily balance of total nitrogen (in g)	Average daily balance of amino nitrogen (in g)
Gr-va	55	14.9	4.6	-10.3	≠2.0
Di-yev	30	17.7	4.3	-13.4	≠1.2
Ba-ov	35	17.0	6.2	-12.1	≠2.1
A-kin	43	19.8	3.2	-12.4	≠3.2
Lu-ov	26	16.8	4.2	-12.7	≠1.5
Va-yev	40	16.4	4.7	-11.7	≠1.8
I-ov	38	16.4	3.0	-13.4	≠1.1
S-ov	34	16.3	2.2	-14.0	≠1.0
Kli-t	52	15.6	4.5	-11.5	≠1.9
Za-ov	44	11.3	3.8	- 7.6	≠1.6
Ku-ov	33	13.5	3.8	- 9.7	≠1.4
Shu-ov	44	12.0	5.3	- 6.7	≠2.1
So-yev	42	12.0	3.2	- 6.8	≠2.1
I-yev	49	8.4	5.8	- 7.9	≠2.2
Go-ov	50	15.5	4.9	- 9.5	≠1.5
Ru-yev	28	17.6	5.3	- 9.2	≠2.5
Sm-ov	34	14.0	4.6	- 7.2	≠2.9
Si-ov	45	12.1	3.7	- 8.4	≠1.7
Ko-in	57	12.8	4.5	- 8.3	≠1.9
Ku-ov	39	14.4	4.6	- 9.8	≠1.9
An-na	41	7.3	4.1	- 3.2	≠1.8
St-na	45	8.1	5.0	- 3.1	≠2.3
Che-va	61	7.9	7.4	- 0.5	≠2.4
Sl-oy	53	3.2	2.2	- 1.0	≠1.5
Pr-va	60	10.2	5.0	- 5.2	--
Average		13.8	4.4	- 8.6	≠2.0

/Continued on next page/

/Table 3 continued from page 47

Change in the protein content in the blood serum	
Protein in the serum before operation	Protein in the serum after operation
7.05%	7.05%
6.9%	7.05%
6.7%	7.35%
--	7.35%
7.05%	6.9%
--	6.9%
--	6.9%
--	6.7%
6.25%	6.5%
5.4%	5.0%
6.6%	

ed either before the operation, or in the postoperative period. The severity of the operative intervention was approximately identical in all patients, no large losses of blood were observed at the time of operation in any case. The content of protein in the blood serum in the patients after the operation and the administration of aminorastin was almost the same as before the operation. We have also noted that the very best results were obtained in exhausted patients. Apparently, the state of the patients and the individual peculiarities of the organism have primary significance in the processes of metabolism.

The following observation can be presented as an example of the assimilability of aminorastin.

Patient P. /female/ was admitted to the clinic on account of cancer of the stomach with stenosis of the pylorus. In view of the fact that she could not eat at all and was strongly emaciated, it was decided to prepare her for operative intervention by the parenteral administration of aminorastin solution. In the course of nine days before the operation the patient was fed only parenterally with aminorastin in a quantity of 750 ml daily in combination with other solvents. In spite of the fact that the quantity of nitrogen being administered was comparatively small (around 5 g per day), and that a weakly negative nitrogen balance was observed (on the average - 2.6g of nitrogen per day), the patient increased in weight by 500 g and endured the operation excellently. It should be noted that this increment in weight was not the result of a holding back of liquid in the organism, since there was no edema in the patient. After the operation of subtotal resection of the stomach for the course of five days the patient received the same parenteral feeding. She was discharged on the 20th day in an excellent state. The loss in weight after operative intervention amounted to 1.9 kg.

One can also judge concerning the assimilation of nitrogenous substances in the organism by the increase in the coefficient which shows the ratio of the nitrogen of the urea to the total nitrogen of the urine. In the case of assimilation of nitrogenous substances by the organism, this coefficient amounts to a value of 0.7-0.9; if the nitrogenous products being administered are excreted from the organism, the coefficient is lowered to 0.4-0.5. When aminorastin was administered the coefficient amounted to a magnitude of 0.76-0.84 in almost all 25 patients. In the patients of the control group, who had not received the solution after the operation, lower values of it were observed (0.4-0.5).

In addition to these investigations, we studied the excretion of amino acids with the urine when aminorastin was administrered. An insignificant quantity of nitrogen is

ordinarily excreted by a human being in the form of amino acids. These basically consist of monoamino acids; the dicarboxylic amino acids -- aspartic and glutamic amino acids -- are ordinarily encountered in the form of traces; the diamino acids are entirely absent. Nevertheless, aminorastin contains all these three groups of amino acids and, if they were not retained in the organism, they could be determined in the urine after the administration of the solution. The amino acid composition of the urine was determined by the method of distribution chromatography on paper. The investigations were conducted in four patients before the administration of aminorastin, during its administration, and also one and three days after the termination of its administration. The results showed that in the presence of the administration of aminorastin and upon the termination of its administration, the amino acids which are usually excreted by healthy individuals could be determined in the urine. The appearance of any other amino acids, including the essential amino acids, was not detected.

Thus, our observations on the use of aminorastin under conditions of clinical practice have shown that the administration of this solution is well endured by patients. Aminorastin does not evoke toxic and antigenic reactions and does not exert any influence on the coagulating system of the blood. The administration of aminorastin to patients in the postoperative period lowers the magnitude of the negative nitrogen balance in comparison with a group of patients who had not received the solution, which is apparently evidence of the assimilation of the nitrogenous substances being administered by the organism. After the administration of aminorastin, the appearance of the amino acids which have important physiological significance is not observed in the urine.

In taking account of the results of our observations, we consider it possible to recommend aminorastin for the parenteral feeding of surgical patients along with other protein hydrolyzates.

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